STUDY ON
SICK EUTHYROID SYNDROME IN ACUTE PESTICIDE POISONING

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THE TAMIL NADU DR. MGR MEDICAL UNIVERSITY

CHENNAI-600 032.

MARCH 2010

CERTIFICATE

This is to certify that the dissertation entitled "STUDY ON **SICK EUTHYROID SYNDROME IN ACUTE PESTICIDE POISONING"** is a bonafide original work of **Dr. K. THIRUMAL VALAVAN,** in partial fulfillment of the requirements for M.D. Branch -I (Internal Medicine) Examination of theTamilnadu Dr. M.G.R. Medical Univeristy to be held in March 2010.

Director
Institute of Internal Medicine
Madras Medical College &
Govt. General Hospital,
Chennai-600 003.

DEAN
Madras Medical College &
Govt. General Hospital,
Chennai-600 003.

DECLARATION

I, **Dr. K. THIRUMAL VALAVAN,** solemnly declare that the dissertation titled, "STUDY ON **SICK EUTHYROID SYNDROME IN ACUTE PESTICIDE POISONING"** is a bonafide original work done by me at Poison Control Training and Research Centre, Institute of Internal Medicine, Madras Medical College & Govt. General Hospital, During Jan. 2009 to June 2009 under the guidance and supervison of **Prof. C. RAJENDIRAN, M.D.,** Institute of Internal Medicine. This dissertation is submitted to the Tamilnadu Dr.M.G.R. Medical University, towards partial fulfillment of requirement for the award of M.D. Degree (Branch-I) in Internal Medicine.

Place : Chennai.

Date : **(Dr. K. THIRUMAL VALAVAN)**

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CONTENTS

INTRODUCTION

Sick euthyroid syndrome can be described as abnormal findings on thyroid function tests that occur in the setting of a non thyroidal illness (NTI) without preexisting hypothalamic-pituitary and thyroid gland dysfunction.[1-3]

A decreased level of serum total triiodothyronine (T_3) is the most common thyroid function abnormality in patients with acute illness[4] and can be detected within 2 hours after the onset of severe physical stress.[5] As the severity of illness progresses, there is gradual development of a more complex syndrome associated with low levels of T_3 and thyroxine (T_4).[6,7]Levels of thyrotropin (TSH) remain unchanged or slightly reduced. The conversion of the pro-hormone (Thyroxine, T4) to the active form is reduced due to decreased 5'-deiodinase activity peripherally and production of reverse T3 (rT3), the inactive metabolite, is increased.

These thyroid hormone changes may be mediated in part by cytokines or other inflammatory mediators, acting at the level of the hypothalamus and pituitary, the thyroid gland, and the hepatic deiodinase system, as well as on binding of thyroxine to thyroid binding globulin.

It remains unresolved whether the hormone responses in the sick euthyroid syndrome represent part of an adaptive response, which lowers tissue energy requirements in the face of systemic illness, or a maladaptive response, which induces damaging tissue hypothyroidism.

Consequently, the use of thyroid hormone therapy in the sick euthyroid syndrome is controversial.

Recovery from the underlying illness is accompanied by disappearance of the thyroid abnormalities.

Altered thyroid hormone levels have been reported in starvation,acute and chronic medical illnesses, bone marrow transplantation, surgery,trauma, myocardial infarction [4] and, in fact, can be seen in any severe systemic illness.

The more profound the changes in hormone pattern, the poorer the prognosis.[8.]

Sick euthyroid syndrome has also been demonstrated in acute organophosphate poisoning.(9)

The aim of the present investigation were to study the occurrence of Sick Euthyroid syndrome in patients with acute pesticide poisoning [31-32] and to evaluate whether such sick euthyroid syndrome positivity have a prognostic significance in the outcome of acute pesticide poisoning.

REVIEW OF LITERATURE

HISTORY:

In the era of industrial revolution many organophosphorous compounds were synthesized. Organophosphates(OPs)are chemical substances originally produced by the reaction of alcohols and phosphoric acid. As early as 1854, Clermont prepared tetra ethyl pyrophosphate(TEPP). OPC made its mark in modern chemistry when Lange and Krueger recorded the synthesis of di-methyl di-ethyl phosphor fluoridates in 1932[10]. They observed that inhalation of these compounds produced blurring of vision and choking sensation.But OPC as pesticides were produced by a group of German scientists led by Gerhard Schrader,Farben Febriken and bayer 1937.The possibilities of potential chemical warfare with these agents were explored by Nazis in World War II.Indeed Sarin(isoproyl methyl phisphonosluoridate) was used by Iraq agaisnt Kurdish rebels in villages of IRAQ [11].The residues of Sarin were still found in analysis of the soil.In 1944 Schrader synthesized parathion which was widely used as pesticide, In 1870 Fraser developed atropine as an antidote to physostigmine.Collomp in 1949 experimented atropine against mucarinic effects of nerve gas. In 1995 Davies introduced oximes and I.B Wilson confirmed its usefulness in acute OPC poisoning. Namba for the first studied GK-11 an anti Glutamimetic drug as neuro protective agent in OPC in 1997 In 1998 adenosine receptor antagonist role was studied in OPC necessitating further studies.

Historic and new uses of organophosphates:

The first organophosphate was synthesized in 1850.Physostigmine was used to treat glaucoma in the 1870s.By the 1950s,synthetic cholinesterase inhibitors were being used for skeletal muscle and autonomic disorders.Some organophosphates were tried in the treatment of Parkinsonism.

In 1986,testing began for tacrine, the first cholinesterase inhibitor to be tried for Alzheimer disease;it was released for clinical use in 1993.The blood-brain barrier has been the limiting factor in developing a Cholinestrase inhibitor for use in dementia. A new drug, rivastigmine, is now available. Reported adverse effects are nausea and vomiting,with resultant weight loss because of the increase in cholinergic activity .It has been shown to be useful in mild to moderately severe Alzheimer disease.

Recently, pyridostigmine has been tried for the fatigue of post polio syndrome.Unfortunately, the study showed no benefit.

TABKE1 : CLASSIFICATION AND THEIR STRUCTURE

Sl.No.	Common Name	Trade Name
1.	Acephate	Asataf,Orthene,Starthene
2.	Chlorpyrifos	Dursban,Durmet,Lorsban
3.	Dichlorvas	Noovan
4.	Dimethoate	Rogar,Tara909,Fosfamid
5.	Fenitrothian	Surmunion,Nitrophos
6.	Fenthion	Baycid,Baytex
7.	Malathion	Cythion,Chemathion
8.	Methyl Parathion	Metacid,Folitav,
9.	Monocrotophos	Monosron,Nuvacron,Luphos
10.	Phorate	Thimet,Pempart
11.	Parathion	Folidol,Ekatox
12.	Phosphomidan	Dimecron,Famfos
13.	Quinalphos	Ekalux

GENERAL CHEMICAL STRUCTURE

Organophosphorous compounds are bascially esters of phosphoric acid or of phosphorothioc acids[12]. The R denotes either ethyl or methyl group.The organothiophosphates which contains double bonded sulphur group are converted to organophosphates in the liver.Phosphonate contains an alkyl(R-)in place of one alkoxy group(RO-). The X is called the leaving group and is the principal metabolite for species identification.[13].

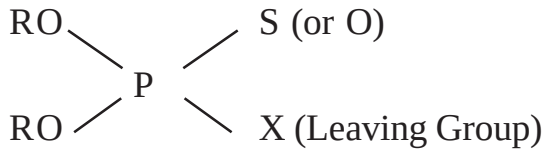


Table 2

Highly toxic:

Sl.no	Brand name	Chemical name
1	Dimecron	Phosphomidan
2	Folidol	Ethyl parathion
3	Celethion	Chlorthiophos
4	Systox	Demeton s methyl
5	Trithion	Carbophenothion
6	Moonbug,metacid	Methylparathion
7	Bloom	Dichlorvas

Moderately toxic :

Sl.no	**Brand name**	**Chemical name**
1	Baytex	Fenthion
2	Entex	Formothion
3	Finit	Malathion
4	Tic 20	Fenitrothion
5	Spectacide	Diazinon
6	Canon,classic 20	Chlorpyriphos
7	Abate	Temephos

Others :

Sl.no	Brand name	Chemical name
1	Hydan,hinosan	Edephenophos
2	Kinadon,siccomedon	Ph osphenidone
3	Josh,Shikari	Triazophos
4	Monocrown,monosul	Monocrotophos
5	Rogor,Digor	Dimethoate
6	Ekalux	Quinalphos
7	Actellic	pirimiphos

KINETICS:

The kinetics of each group are highly dependent upon many factors such as route of administration such as ingestion, inhalation, transdermal and transmucosal exposure,distance from target organ ,local versus systemic metabolisim and activation,route of elimination, endogenous hydrolysis and consumption of the compound by non specific esterases. Each group has its chemical structure, R-groups attached to the sulphur,carbon,or phosphorus entity,tightness of the bond to the central atom and the inherent affinty to cholinesterase .[14] After absorption the chemical are equally distributed in all tissues but predominantly in liver and the renal.Lipophilic compounds reach maximum concentration in neural and other lipid rich tissues. Plasma half life after single dose administration depends upon the type of opc and route of exposure and it may range from few minutes to

few hours.Metabolism occurs mainly by three ways namely oxidation, hydrolysis by esterases and transfer of portion of molecule to glutathione. Urinary and faecal excretion occurs in 48 hours where in 80-90% of the compund is eliminated [15]. Most of the agents show some symptoms and signs within six to ten hours[16] with the exception of fat soluble compounds where it may take several days to weeks to manifest because the substance must be leached out of the fat. Some opc have to be activated to active toxic state(hepatic activation of parathion to paraxon).Studies reveal that these residues may remain for days to week even after treatment.[17]

MECHANISM OF ACTION:

Acetylcholine (ACh) is the neurotransmitter released at all postganglionic parasympathetic nerve endings and at the synapses of both sympathetic and parasympathetic ganglia.It is also released at the skeletal muscle myoneural junction,and serves as a neurotransmitter in the central nervous system.ACh is hydrolyzed by acetyl cholinesterase into two fragments:acetic acid and choline.

Acetyl cholinesterase is present in two forms: True acetyl cholinesterase which is found primarily in the tissues and erythrocytes,and pseudo cholinesterase which is found in the serum and liver.

Organophosphorous compounds are acid-transferring inhibitors of cholinesterase.They cause cholinesterase to become firmly(and sometimes irreversibly) phosphorylated.This means that the action cholinesterase will be inhibited.Cleavage of the carbon-enzyme bond form ACh is complete

in a few microseconds. However,the breaking of the phosphorous-enzyme bond requires a period varying from 60 minutes to several weeks,depending on the organophosphorous compound involved.

Reactivation of the inhibited enzyme may occur spontaneously.The rate of reactivation will depend on the species,the tissue,and the chemical group attached to the enzyme.Reactivation may be enhanced by hydrolysis of the acid-radical-enzyme through the use of oximes(i.e. reactivation agents).Response to reactivating agent is declining with time.This process is being caused by''ageing'' of the inhibited enzyme.Ageing is probably the result of the loss of one alkyl or alkoxy group,leaving a much more stable acetyl cholinesterase.The aged phosphorylated enzyme cannot be reactivated by oximes.

Accumulation of acetylcholine causes overstimulation of both muscarinic and nicotinic receptors,and subsequently disrupts the transmission of nerve impulses in both the peripheral and central nervous system.[17]

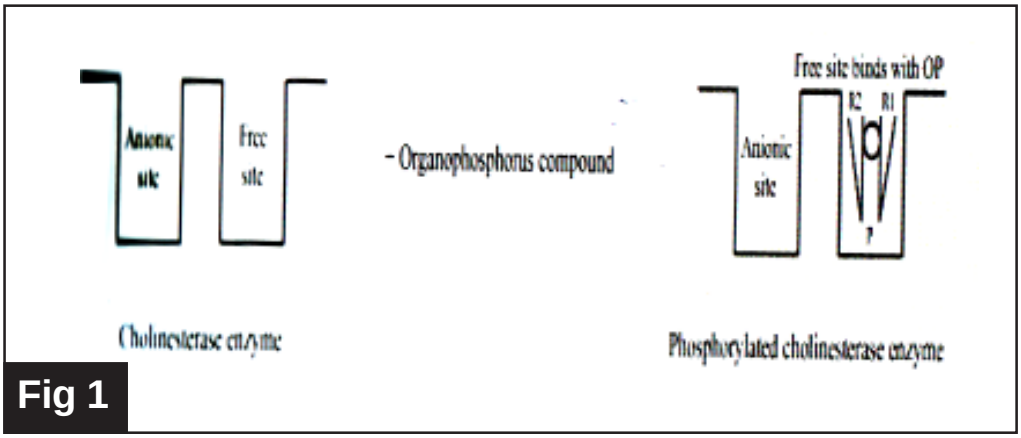
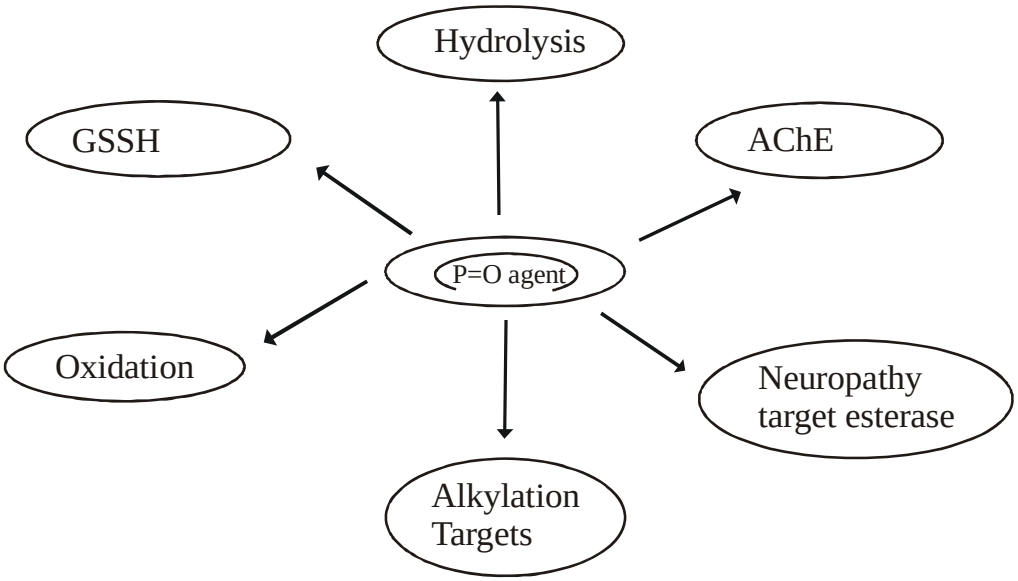


Fig 1

Most of these OPC do not posses a positive charge;hence they react with esteratic site but not with anionic site.Splitting of the acid group then occurs.

The bond between phosphorous and esteratic site(free site) is more stable than the bond between carbon atom acetyl choline and the same site.Thus blocking of the active site and consequent inactivation of enzymes results in accumulation of acetylcholine at cholinergic sites.Pseudo cholinesterase is a less specialized enzyme as it lacks an anionic site in a position that specially adapts it to react with acetylcholine.It does however react with acetyl choline, albeit, more slowly and also with a wide range of other esters.

BIOLOGICAL INTERACTIONS OF OPC [18].



CLINICAL FEATURES

The clinical features depend upon the end points were sustained cholinergic stimulation takes palce namely

a. Post ganglionic parasympathetic hollow end organ(muscarinic)

b. Sympathetic and parasympathetic ganglionic and somatic neuro mucsular junction(nicotinic)

c. Central nervous system affection[19]

Following exposure to organophosphorous compounds,the toxic features are usually obvious within 30 minutes to 3 hours.This may be delayed in some cases depending on the rate and amount of systematic absorption.The majority of patients give a history of intentional or accidental ingestion of organophosphorous compunds.Toxcity is produced by the rapid absorption of the compound through the gastrointestinal,respiratory tracts and skin.

The clinical symptoms and signs are non-specific and will depend on the specific agent,the quantity and the route of entry.Some patients present with vomiting,diarrhea and abdomianl pain,whilst others may be unconscious on arrival at the hospital.A high index of suspicion is therefore needed to make an early diagnosis. Early cases present predominantly with parasympathetic over-activity, and a charasteristic garlic smell.The end result may be multi-system manifestation involving the gastrointestinal, reapiratory,and cardovascular and nervous systems,as well as involvement of skeletal muscle, other organs and metabolic effects such as hypo or hyperglycemia.Most fatalities occur within 24 hours and those who recover usually do so within 10 days.

CARDIAC MANIFESTATIONS:

The commonest cardiac manifestations following poisoning are hypotension (with warm,dilated peripheries),and bradycardia.Patients seldom present with tachycardia and hypertension due to predominant nicotinic receptor blockade.Cardiac manifestations are often the cause of serious complications and fatality.[20].

Table3. Symptoms and signs of organophosphorous poisoning

Muscarinic receptors	Nicotinic receptors	Central receptors
Cardiovascular • Bradycardia • Hypotension **Respiratory** • Rhinorrhoea • Bronchorrhoea • Bronchospasm • Cough **Gastrointestinal** • Nausea/vomiting • Increased salivation • Abdominal cramps • Diarrhea • Faecal incontinence **Geniturinary** • Urinary continence **Eyes** • Blurred vision • Increased Lacrimation • Miosis **Glands** • Excessive salivation	**Cardiovascular** • Tachycardia • Hypotension **Muscuskeletal** • Weakness • Fasciculation • Cramps • Paralysis	**General effects** • Anxiety • Restlessness • Ataxia • Comvulsions • Insomnia • Tremors • Coma • Absent reflexes • Respiratory depression • Circulatory collapse

The mechanism of cardiac toxicity is unclear and the following has been postulated:

- A direct toxic effect on the myocardium
- Over activity of cholinergic or nicotinic receptors causing hemodynamic alteration
- Hypoxia
- Acidosis
- Electrolyte abnormalities
- High dose atropine therapy (used as treatment for organophosphate poisoning)

RESPIRATORY MANIFESTATIONS :

Respiratory manifestations of acute organophosphorous poisoning include bronchorrhoea,rhinorrhoea,bronchospasm and laryngeal spasm.This is due to the action of the organophosphate on muscarinic receptors.The intergrity of the airway may be compromised by excessive secretions.The nicotinic effects lead to weakness and subsequent paralysis of respiratory and oropharyngeal muscles.This increases the likehood of both airway obstruction and aspiration of gastric contents. Finally,central neurological depression may lead to respiratory arrest.

GASTROINTESTINAL MANIFESTATIONS :

Symptoms resembling gastroenterities such as vomiting, diarrhea and abdominal cramps are the first to occur after oral ingestion of an organophosphorous compound.

NEUROLOGICAL MANIFESTATIONS :

A large number of patients, following acute exposure to organophosphorous compounds, require prolonged ventilatory support in the intensive care unit due to neuromuscular weakness. The neurological menifestations have therefore been a primary focus of interest. There has been an emphasis on reducing the incidence of neuro - muscular respiratory failure. Three different types of paralysis are recognized based largely on the time of occurance and their differing pathophysiology :

- Type I Paralysis or acute paralysis
- Type II Paralysis or Intermediate Syndrome
- Thpe III Paralysis or Organophosphate - induced delayed polyneuropathy.

ENDOCRINE CHANGES IN PESTICIDES

In critical illness, several drugs and various stressful conditions modify the functions of neurotransmitters which consequently affect the secretion of pituitary hormones. Although the role of neurotransmitters in the regulation endocrine system is well known, cholinergic actions have been

less investigated. Organophosphoate compounds may result in sick euthyroid syndrome. These conditions may be related to the effects of acetylcholine and direct effect of organophosphate compounds. Cholinesterase inhibitors were shown to modify the pituitary-thyroid and pituitary- adrenal axes. Pesticides such as soman have been shown to produce a significant increase in serum corticosterone, thyroxine, and triidothyronine concentrations after poisoning. Thyroid function in pregnant womem is a critical determinant of offspring's IQ and contaminants such as polychlorinated biphenyls and dioxins are known to disrupt thyroid function. Such findings demonstrate the special sensitives of developing embryos and fetuses to chemical exposure levels that are safe and without effect in mature adults.

OTHER EFFECTS OF OPC MAY INCLUDE

- Neuropsychiatric effects : Impaied memory, confusion, irritability, lethargy, psychosis and chronic organophosphate- induced Neuropsychiatric disorders have been repored. The mechanism is not proven. [21]

- Extra pyramidal effects : These are characterized by dystonia, cogwheel rigidity, and parkinsonian features (Basal ganglia impairment after recovery from acute toxicity).

- Other neurological and / or psychological effects : Guillain - Barre-like syndrome and isolated bilateral recurrent laryngeal nerve palsy are possible.[22]

- Ophthalmic effects : Optic neuropathy, retinal degeneration, defective vertical smooth pursuit, myopia and miosis (due to direct ocular exposure to organphosphates), are possible.

- Ears: Ototoxicity is also possible[23].

MODIFIED DREIBACH'CLINICAL CRITERIA - KARNIT [24]

GRADE I - Mild symptoms related to portal of entry.

Nausea,vomiting in case of ingestion

Cough,burning sensation in the chest in case of inhalation
Mild systematic symptoms like headache, Dizziness, weakness

GRADE II - Moderate systematic intoxication

Abdominal pain and diarrhea in case of ingestion.

Tightness in chest,difficulty in breathing in case of inhalation

Salivation, Lacrimation, Sweating, Pupillary changes. Bradycardia, confusion, tremor, restlessnes.

GRADE III - Severe systemic intoxication

Respiratory depression,generalized weakness

Cyanosis, peripheral circulatory failure,

Convulsion,coma.

DIAGNOSTIC CRITERIA[19]

- **INVESTIGATORY MODALITES:ESTIMATION OF CHOLINESTERASE LEVELS:**Organophosphate (OP) toxicity is a clinical diagnosis.Confirmation of organophosphate poisining is based on the measurement of cholinesterase activity;typically,these resluts are not readily available.Altough RBC and plasma (pseudo)cholinesterase levels can both be used,RBC cholinesterase correlates better with CNS acetyl cholinesterase (AChe) and is,therefore,a more useful marker of organophosphate poisoning.

    - Meauremaent of RBC and plasma cholinesterase levels prior to treatment with pralidoxime (2-PAM).Monitoring serial levels can be used to determine a response to therapy.

    - RBC AChE represents the AChE found on RBC membranes,similar to that found in neuronal

tissue.Therefore, RBC AchE measurement more accurately reflects nervous system OP AChE inhibition.

- Plasma cholinesterase is a liver acute-phase protein that circulates in the blood plasma.It is found in CNS. White matter,the pancreas,and the heart. It can be affected by many factors, including pregnancy,infection, and medical illness. Additionally, a patient's levels can vary up to 50% with repeated testing.

- RBC cholinesterase is the more accurate of the 2 measurements,but plasma cholinesterase is easier to assay and is more readily available.

- Cholinesterase levels do not always correlate with severity of clinical illness.

- The level of cholinesterase activity is relative and is based on population estimates.Neonates and infants have baseline levels that are lower than adults.Because most patients do not know their baseline level ,the diagnosis can be confirmed by observing a progressive increase in the cholinesterase value until the value plateau over time.

- Falsely depressed levels of erythrocyte cholinesterase can be found in pernicious anemia,hemoglobinopathies,use of antimalarial drugs,and oxalate blood tubes.

- Falsely depressed levels of plasma cholinesterase are obreserved in liver dysfunction,low- protein conditions, neoplasia,hypersenstivity reactions,use of certain drugs (succinylcholine,codeine,and morphine), pregnancy,and genetic deficiencies.

- Other laboratory findings include leukocytosis, hemoconcentration, metabolic acidosis, hyperglycemia, hypokalemia, and hypomagnesemia.

IMAGING STUDIES

A chest radiograph may reveal pulmonary edema but typically adds little to the clinical management of a poisoned patient. Electrocardiographic manifestations include prolonged Q-Tc intervals, elevation of the ST segment, inverted T waves and a prolonged PR interval. There may also be rhythm abnormalities such as sinus bradycardia, ventricular extra-systoles, ventricular tachycardia and fibrillation. Ludomirsky et al described three phases of cardiac toxicity following organophosphate poisoning :

- **Phase I :** A brief period of increased symphathetic tone.
- **Phase II :** A prolonged period of parasympathetic activity including AV node blockade

- **Phase III :** Q-T prolongation followed by torsades de pointes, ventricular tachycardia and ventricular fibrillation [25]

THERAPEUTIC CONSIDERATIONS

Medical Care : Airway control and adequate oxygenation are paramount in organophosphate poisonings. Intubations may be necessary in cases of respiratory distress due to laryngospasm, bronchospasm, bronchorrhoea, or seizures. Immediate aggressive use of atropine may eliminate the need for intubation. [26] Succinylcholine should be avoided because it is degraded by acetyl cholinesterase (AChE) and may result in prolonged paralysis.

- Continuous cardiac monitoring and pulse oximetry should be established; an ECG should be performed. Torsades de Pointes should be treated in the standard manner. The use of intraenous magnesium sulfate has been reported as beneficial for organophosphate toxicity. [27] The mechanism of action may involve acetylcholine antagonism or ventricular membrance stabilization.

- Remove all clothing and gently cleanse patients suspected of organophosphate exposure with soap and water because organophosphates are hydrolyzed readily in aqueous solutions with a high pH. Consider clothing hazardous waste and discard accordingly.

- Health care providers must avoid contaminating themselves while handling patients. Use personal protective equipment, such as neoprene or nitrile gloves and gowns, when decontaminating patients because hydrocarbons can penetrate non polar substances such as latex and vinyl. Use charcoal catridge masks for respiratory protection when decontaminating patients who are significantly contaminated.

- Irrigate the eyes of patients who have ocular exposure using isotonic saline.

- If ingestion occured within 30 to 60 minutes placement of nasogastric tube and administration of activated charcoal in a dose, 1g / kg orally. Cathartics are contraindicated because of electrolyte imbalance. [28]

Atropine administration : 3-5mg rapid intravenous should be given to reach effective atropinisation. The adequate atropinisation is gauged by five paramenters.

1. Pulse rate > 85 / min
2. Systolic blood pressure> 80mm Hg
3. Absence of lung crackles.
4. Dry axilla.
5. No constricted pupils [20]

Then after three to five minutes, if the parameters are not attained, double the initial dosing. Atropine should be given in doubling dose pattern till adequate atropinisation.

Maintenance of atropinisation: 10-20% of the bolus dose should be given as infusion in 100ml normal saline and the parameters are assessed every 15 miniutes. If there is inadequate atropinisation superimposed bolus in the dosage of 3-5 mg should be given. Atropine should be tailored down hourly for six hours and then every two to three hours for the next 24hrs. Meticulous watch for atropine toxicity such as agitation, confusion, retention of bladder, hyperthermia, ileus and tachycardia should be done.

Glycopyrrolate can be used instead of atropine. It does not raise the heart rate [49].

OXIMES : PRALIDOXIME (2-PAM OR PROTO PAM) [29]

Cholinesterase reactivation

Oximes are nucleophilic agents that re-activate the phosphorylated acetyl cholinesterase by binding to the organophosphorous molecule. The use of oximes in acute organophosphorous poisoning has been a controversial subject for the last two decades as there have been very few randomized controlled trials that have addressed the role of pralidoxime (PAM).

Pralidoxime has three main actions.

- A direct reaction converting the organophosphate to a harmless compound.
- A transient reaction protecting the enzyme from further inhibition.
- Reactivation of the inhibited alkyl phosphorylated enzyme to free the active unit (if given early enough)

The reactivating action of pralidoxime is most marked at the nicotinic skeletal neuromuscular junction. It does not reverse the muscarinic manifestations of organophosphorous poisoning. Pralidoxime should be started as early as possible to prevent permanent binding of the organophosphate to acetyl cholinesterase. Once this has occured, receptor regeneration is required to allow recovery. The recommended dose of pralidoxime in organophosphorous poisoning is 500 mg/hr infusion for the first 48 hrs. followed by 1 gm in tds for another 3 days. Pralidoxime should be continued until adequate spontaneous ventilation is achieved by the patient. The effective plasma concentration is 4mg / litre and the patient should show signs of improvement 10-40 minutes after its administration. Plasma and pseudo cholinesterase levels should ideally be monitored during treatment. Side effects of pralidoxime include drowsiness, visual disturbances, nausea, tachycarida and muscle weakness, so treatment should be reserved for potentially fatal cases. Fresh frozen plasma can also be used in the management of OPC [50].

PREVENTION AND EDUCATION

Improved regulation of the availability of pesticides, strict regulation of vendors, and modifications in packaging of pesticides may all help reduce the use of organophosphates as poisons. Adequate provision of information to the public, regular training of health care providers, better availability of drugs/antidotes and the establishment of poison information centers will facilitate in reducing the morbidity and mortality related to organophosphorous poisoning. Insecticides should be kept out of reach of children, to prevent accidental poisoning. During agricultural spraying, proper precautions should be taken to prevent inhalation. Accidental ingestion was reported from Japan where there were 19,436 cases over a period of 17 years (1953-1969). WHO used data from 19 countries and reported approximately 5,00,000 cases of pesticide poisoning annually. Of these 99% belong to third world countries[29]. In 1981 the estimate was 75,000 cases annual and rose to 3 million in 1983 and majority were under the age of 30 [30]. Pesticide poisoning contributes more than forty percent of cases in Poison Centre GGH Chennai. The mortality rate due to this poison is 42.29% (case register 2001-2004). The victims are farmers of rural South India.

OBJECTIVES

1. To describe the epidemiology of Pesticide poisoning in poison centre, Government General Hospital, Chennai.

2. To Study the clinical profile of Pesticide poisoning in poison Centre, Government General Hospital, Chennai.

3. To analyze the epidemiological and clinical factors in correlation to severity and outcome of pesticide in poison centre, Government General Hospital, Chennai.

4. To analyse the incidence of sick Euthyroid syndrome in patients admited with pesticide poisoning in Poison Centre Government General Hospital, Chennai.

5. To study the correlation between the incidence of sick Euthyroid syndrome and its assocation with out come.

MATERIALS AND METHOD

SETTING :

This study was conducted in the Poison control, training and research Centre, GGH, Chennai in collaboration of Institute of Internal Medicine Institute of Biochemistry. It was a prospective study done during the period from Jan 2009 - June 2009.

INCLUSION CRITERIA :

60 Patients with history and clinical features suggestive of Pesticide poisoning were selected irrespective of age and sex.

Ethical Clearance - obtained

Informed Concern -Obtained.

EXCLUSION CRITERIA :

1. Patient with past or present H/o. thyroid Dysfuntion
2. Patients taking drugs that will affect thyroid function
3. Patients with liver disease
4. Patients with Renal Dysfuntion.
5. Patients with poisoning whose compound were not known.

Patients with known history of exposure to organophosphorous compounds were taken into consideration. The reliability on exposure was reinforced by definite history from the patients and their attendants. The container from which the poison were consumed were studied for the type and the quantity estimated. Each patient registered for the study went through deatiled clinical evaluation as per the proforma. The cases were divided into three groups as mild, moderate and severe by modified DREISBACH criteria. All patients underwent baseline laoratory investigations. The gastric aspirate was analyzed by thin layer chromatography method for the detection of poison.

All patients underwent complete hemogram, renal function test, liver function test, ECG, Chest roentgenogram, and thyroid function status and serum cholrine esterase.

The other biochemical markers such as liver enzymes and amylase were taken on day 1.

BIOCHEMICAL MARKERS AND THE METHODS EMPLOYED (KITS)

1. CHOLINESTERASE - KITNETIC COLORIMETRIC METHOD [31]
2. SGOT (AST) - UV KINETIC METHOD [32]

3. SGPT - (MODIFIED IFCC METHOD) [33]

4. ALKALINE PHOSPHATASE - PNPP METHOD [34]

Ventilatory Support was considered in patients with following parameters.

a. RR > 35/min

b. Apnea or obvious hypoventilation

c. Persistent cyanosis, excessive secretions, depressed level of consciousness, inability to protect the air way [34]

d. PaO2 < 60mmHg, FiO2 <0.6

PaCO2 > 50mmHg, pH <7.2

Mechanical ventilation was performed with assist control mode and SIMV either as volume or pressure control. Positive end expiratory pressure was titrated to keep SaO_2 above 94% with 40% FIO_2. Weaning was performed using either T-tube trials or pressure support weaning. All patients were monitored meticulously and vital signs assessed till the outcome.

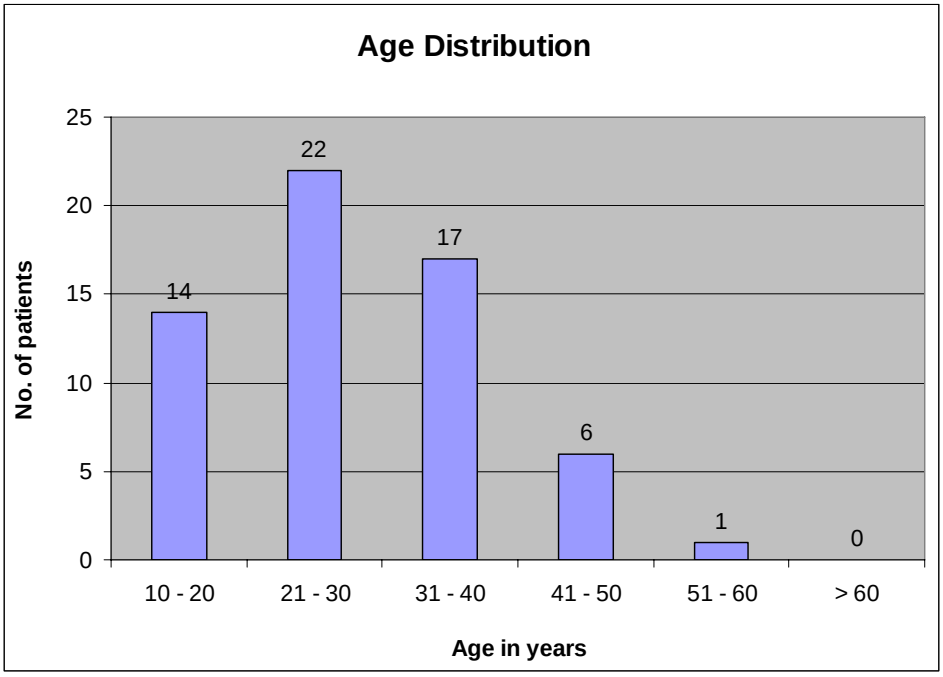
Detailed evaluation of each patient was made. Each variable in the proforma was correlated with severity and mortality.

RESULTS

Epidemiological Pattern of Pesticides in Poision Centre, Govt. General Hospital

Age Distribution

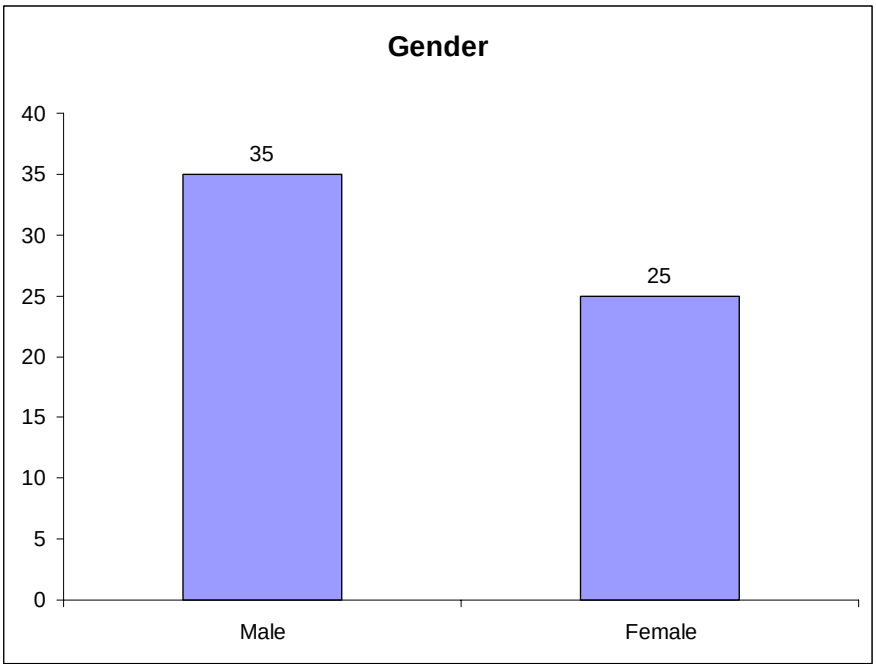
Sl.No.	Age Group in Years	Frequency (n)	Percentage
1.	< 20	14	23
2.	21-30	22	37
3.	31-40	17	28
4.	41-50	6	10
5.	51-60	1	2
6.	> 60		
	TOTAL	**60**	**100**

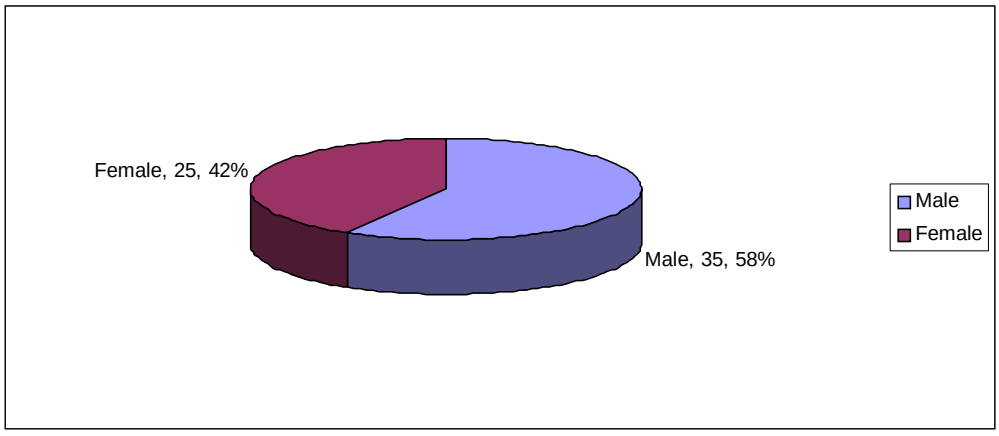


Majority of Patients were in 21-30 Age Group. The Number of Patients between the age group 20 - 40 accounts for 65%

GENDER

Sl.No.	Sex	Frequency (n)	Percentage
1.	Male	35	58.4
2.	Female	25	41.6
	TOTAL	**60**	**100**

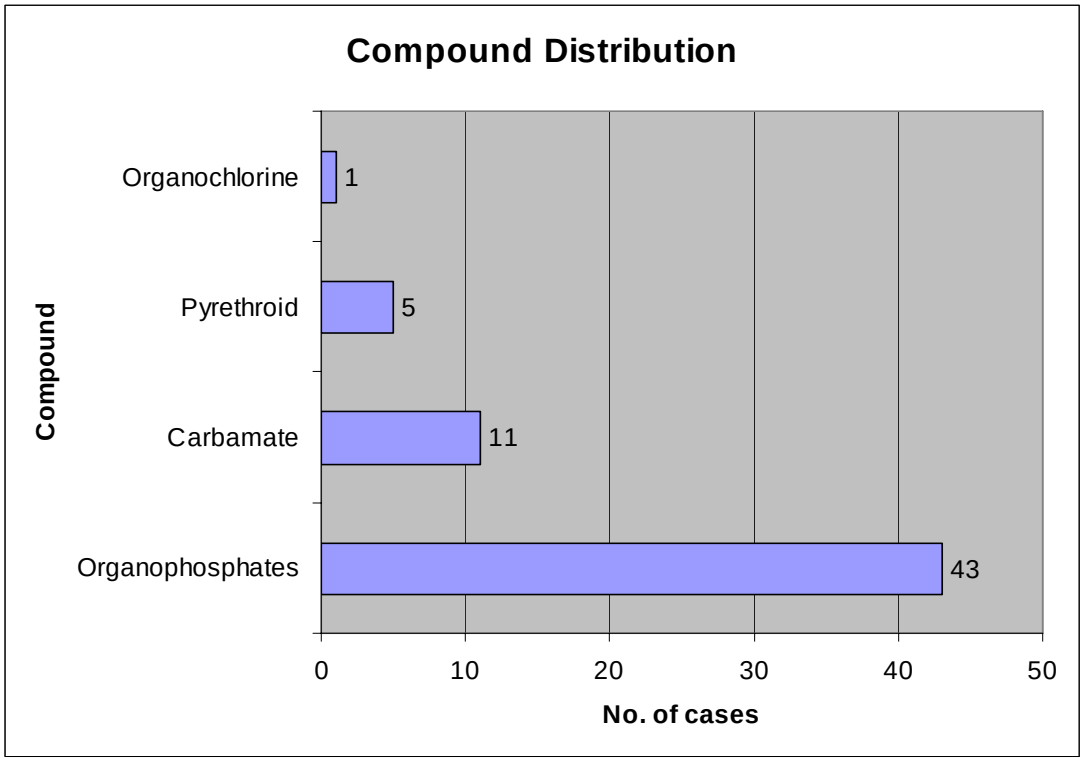




Incidence of Poisioning was more in males when compared to females in our Series 35out of 60 are males.

COMPOUND DISTRIBUTION AMONG PESTICIDES

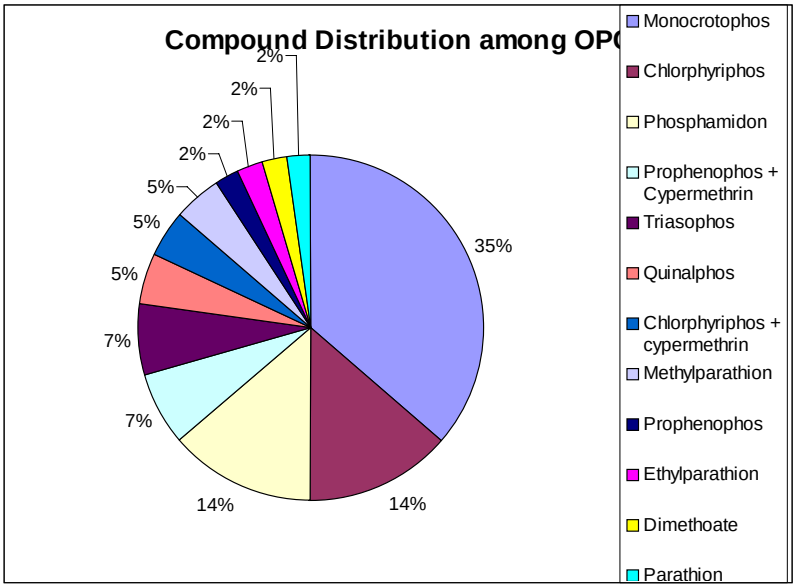
Sl.No.	Compound	Frequency (n)
1.	Organophosphates	43
2.	Carbamate	11
3.	Pyrethroid	5
4.	Organochlorine	1
	TOTAl	**60**



Among the pesticides the most common compound consumed was orgnophosphates.

COMPOUND DISTRIBUTION AMONG OPC

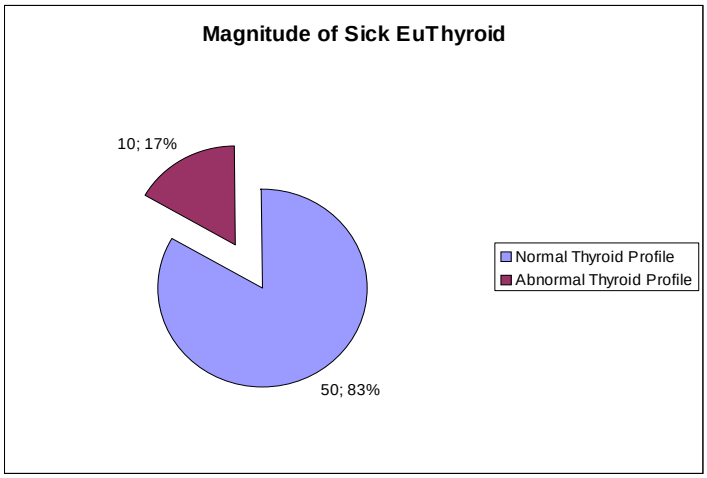
Compound	Nos.	Percentage
Monocrotophos	16	35
Chlorphyriphos	6	14
Phosphamidon	6	14
Prophenophos + Cypermethrin	3	7
Triasophos	3	7
Quinalphos	2	5
Chlorphyriphos + cypermethrin	2	5
Methylparathion	2	5
Prophenophos	1	2
Ethylparathion	1	2
Dimethoate	1	2
Parathion	1	2

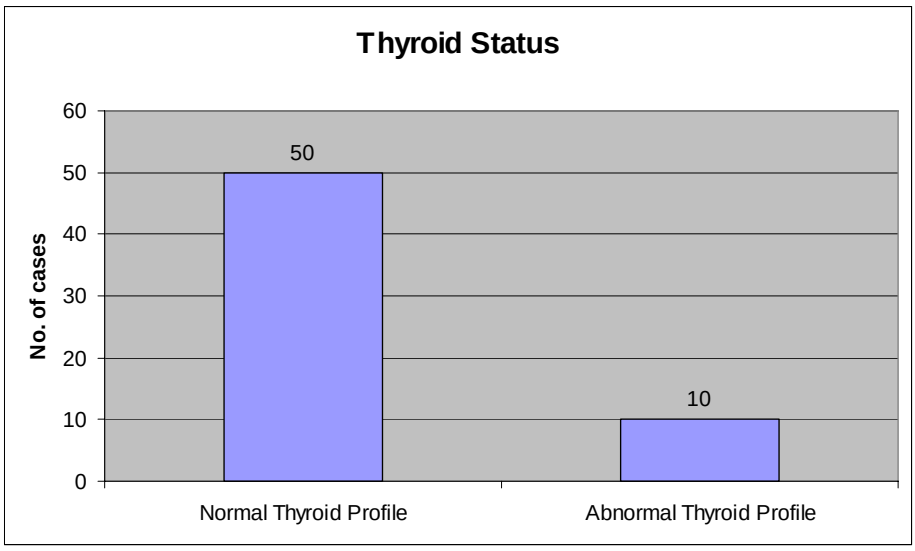


Most Common Compound among OPC was monocrotophos.

MAGNITUDE OF SICK EUTHYROID

	Nos.	Percentage
Normal Thyroid	50	83
Sick Euthyroid	10	17

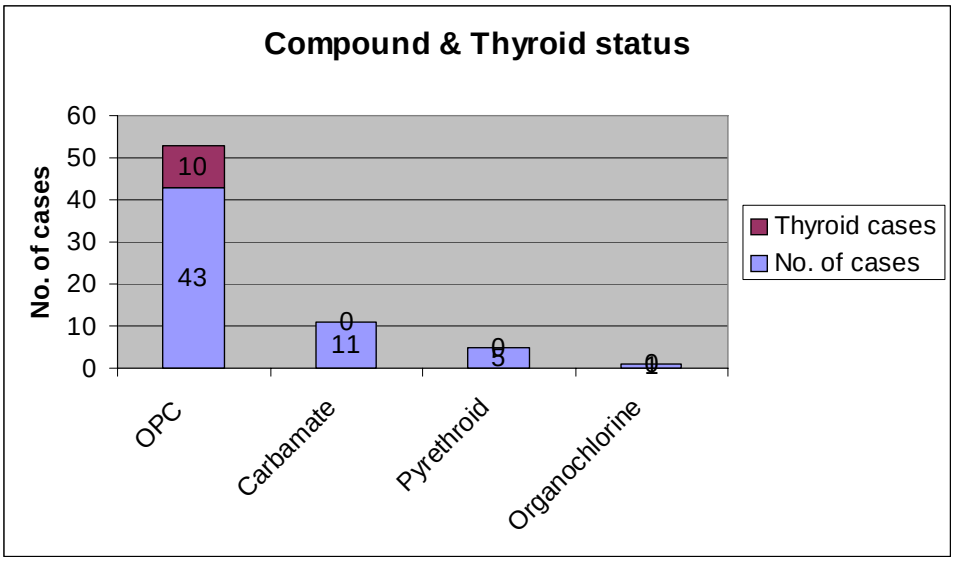


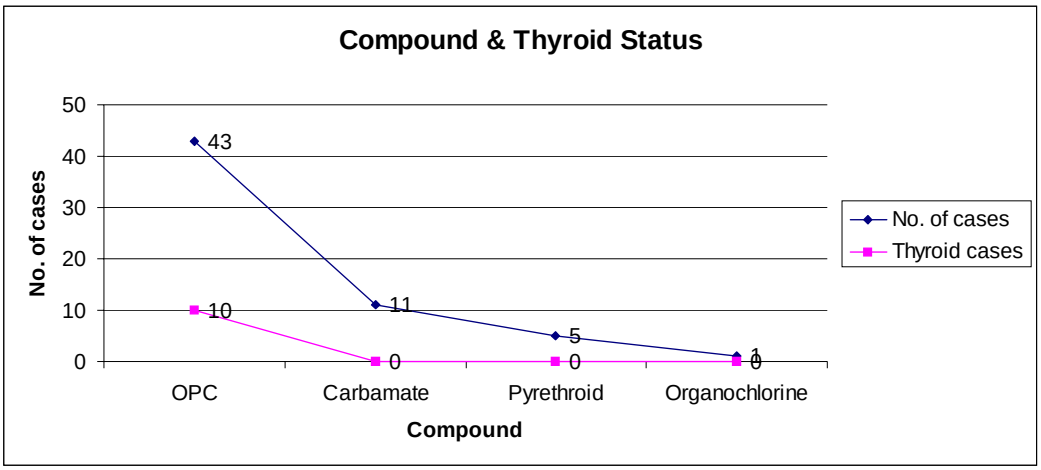


Among the 60 patients studied sick Euthyroid was noted in 10 patients.

COMPOUND & THYROID STATUS

Compound	No. of cases	Sick Euthyroid
OPC	43	10
Carbamate	11	Nil
Pyrethroid	5	Nil
Organochlorine	1	Nil

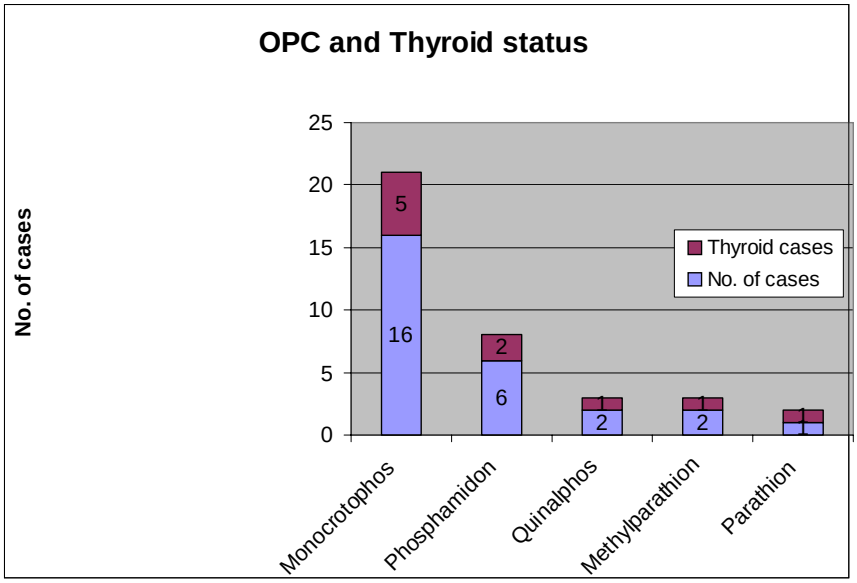


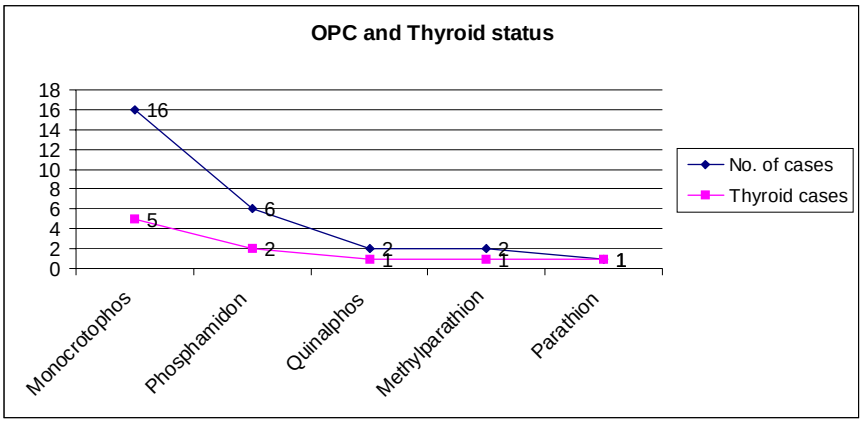


Among the 60 paitents who were studied, sick Euthyroid status was noted only among 10 patients with OPC Poisioning.

OPC AND THYROID STATUS

	Nos.	Death
Monocrotophos	16	5
Phosphamidon	6	2
Quinalphos	2	1
Methylparathion	2	1
Parathion	1	1

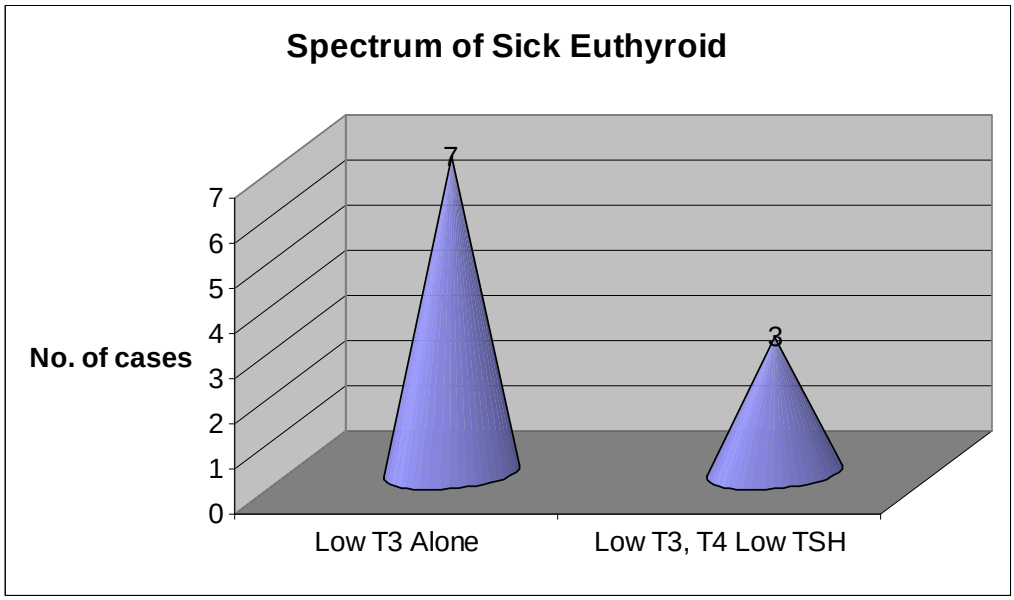


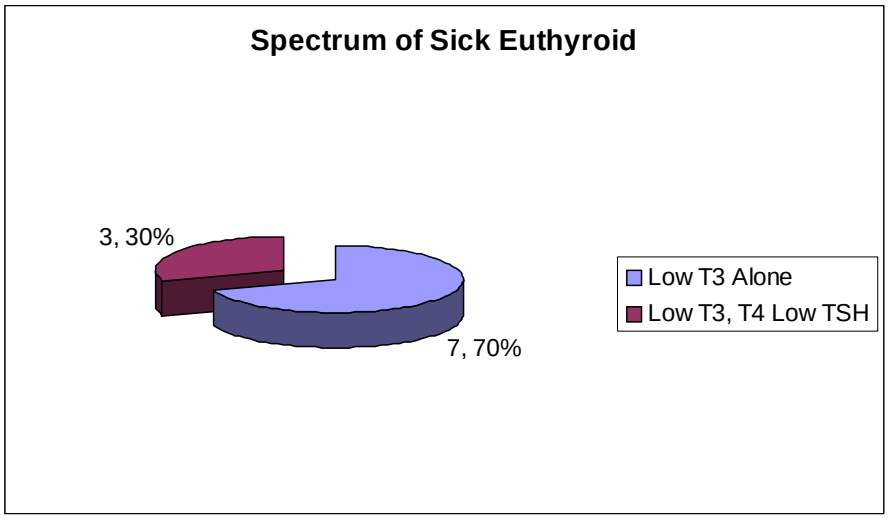


Among the 43 Patients with OPC Poisioning Sick Euthyroid status was noted in 10 Patients. Maximum was among Monocrotophos poisioning.

SPECTRUM OF SICK EUTHYORID

Spectrum	No.	Percentage
Low T3 Alone	7	70
Low T3, T4 Low TSH	3	30

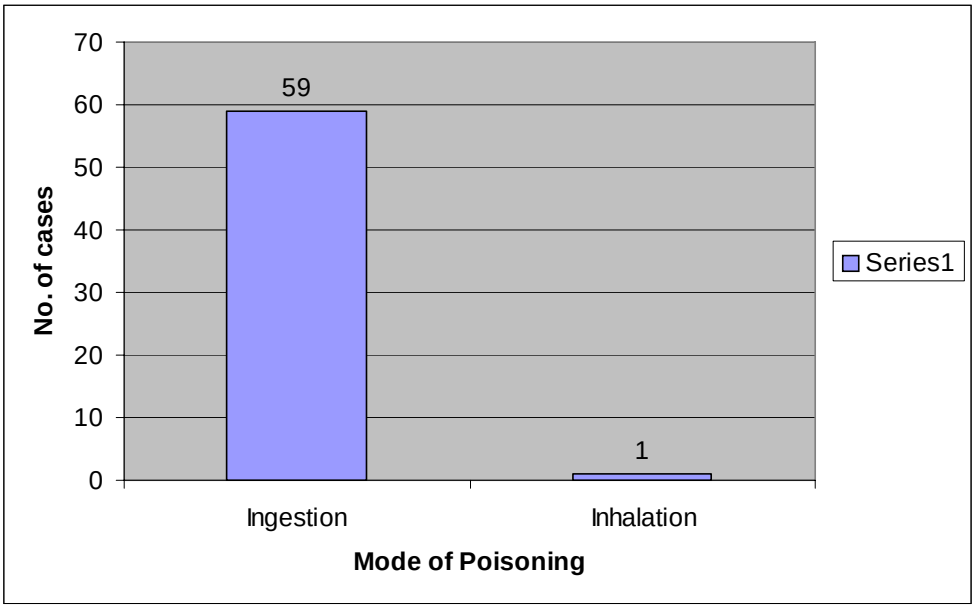


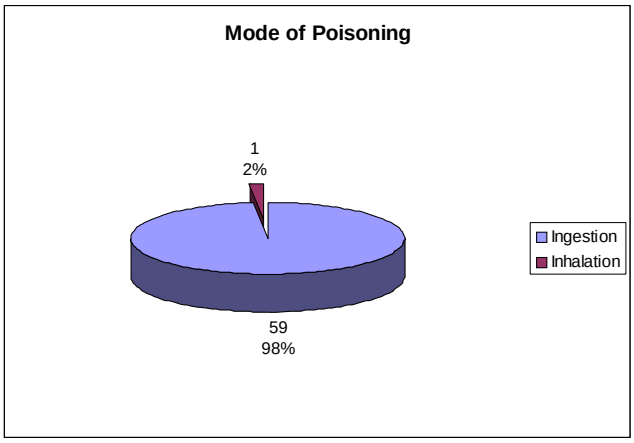


Among the 10 patients with sick Euthyroid, Low T3 alone was noted in 7 patients. 3 patients had changes in T3, T4 & TSH Levels.

ROUTE OF EXPOSURE

Sl.No.	Route of Exposure	Frequency (n)	Percentage
1.	Ingestion	59	98
2.	Inhalation	1	2
	TOTAL	**60**	**100**

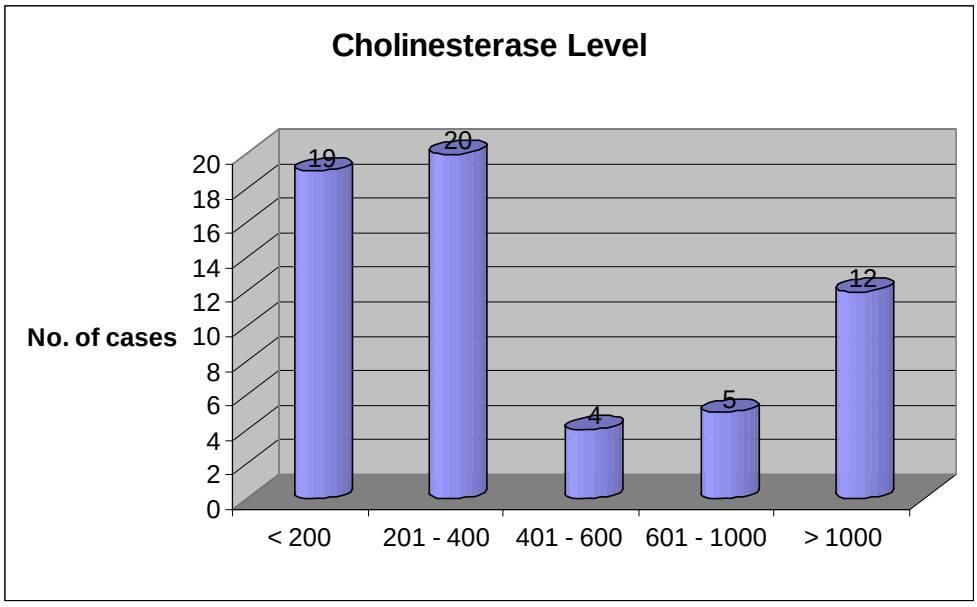




Ingestional exposure was more common in this series.

CHOLINESTERASE LEVEL

Values	Nos.	Percentage
< 200	19	32
201 - 400	20	33
401 - 600	4	7
601 - 1000	5	8
> 1000	12	20

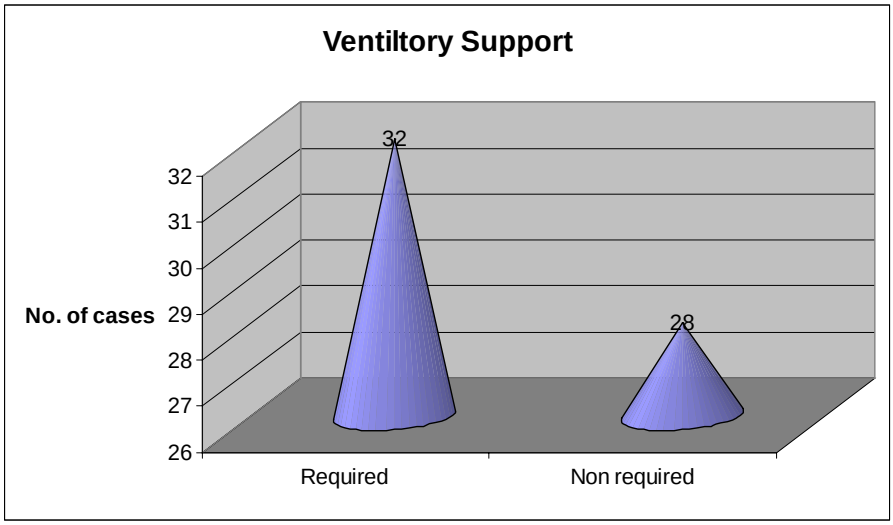


THYROID	N	MEAN	STD. DEVIATION
NEG	50	1405.0600	2118.77612
POS	10	217.6000	71.04803
TOTAL	60	1207.1500	1981.98386

The Mean cholinesteras level was 1207. Among sick Eu Thyroid the mean level was 217 which was much lower when compared to patients with no Thyroid abnormality.

VENTILATORY SUPPORT

		Percentage
Required	32	53
Non Required	28	47



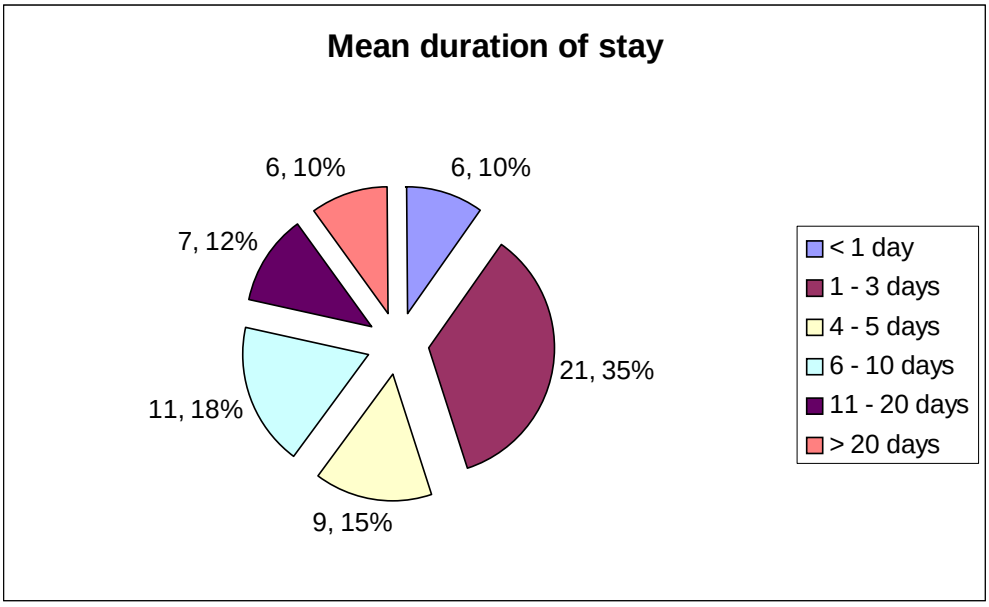
Thyroid Status & Ventilator

		NO	YES
NEG		28	22
POS			10

Ventilator was required in 53% of total Patients admitted. All those with sick eu thyroid were in need of ventilatory support.

DURATION OF STAY IN HOSPITAL

Values	Nos.	Percentage
< 1 day	6	10
1 - 3 days	21	35
4 - 5 days	9	15
6 - 10 days	11	18
11 - 20 days	7	12
> 20 days	6	10

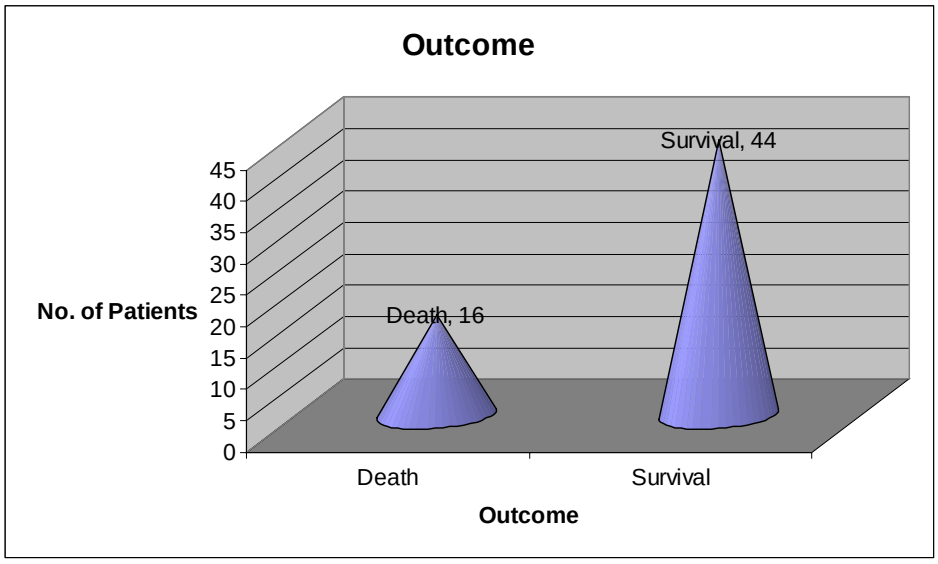


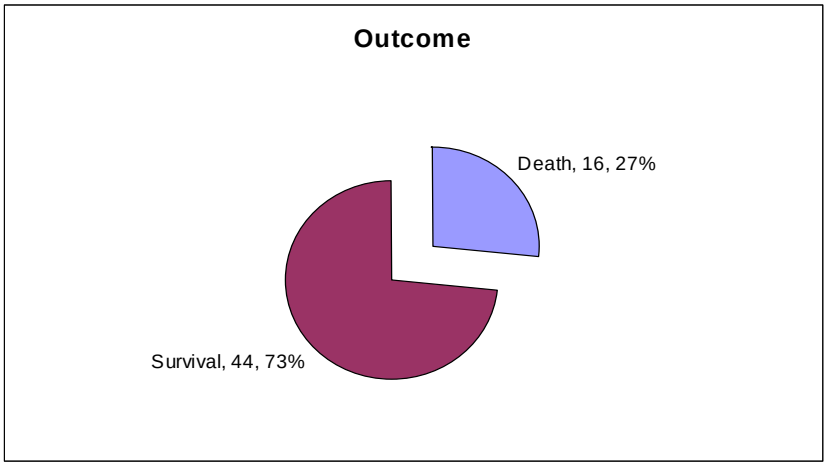
THY	MEAN	N	STD. DEVIATION
NEG	4.9000	50	4.14655
POS	15.3000	10	9.84378
TOTAL	6.6333	60	6.65867

The Mean duration of stay among patients was 6.6333. Among those with sick Eu thyroid the mean duration of stay was 15.3 which was significantly longer than those who were negative for thyroid status.

OUTCOME

	Nos.	Percentage
Death	16	27
Survival	44	73

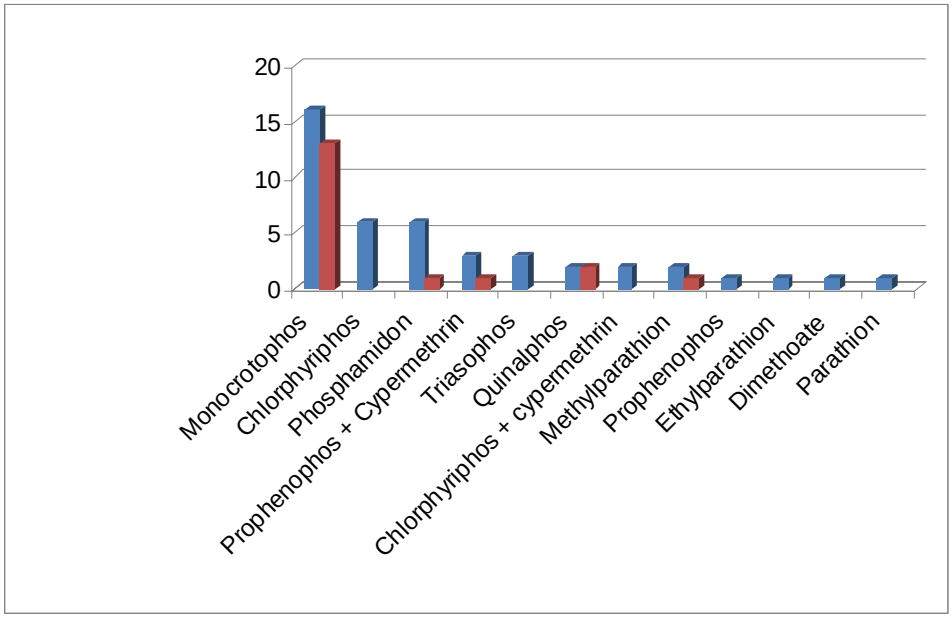




Among the 60 patients studied 16 of them died. The Mortality rate was 27 %.

COMPOUND AND MORTALITY

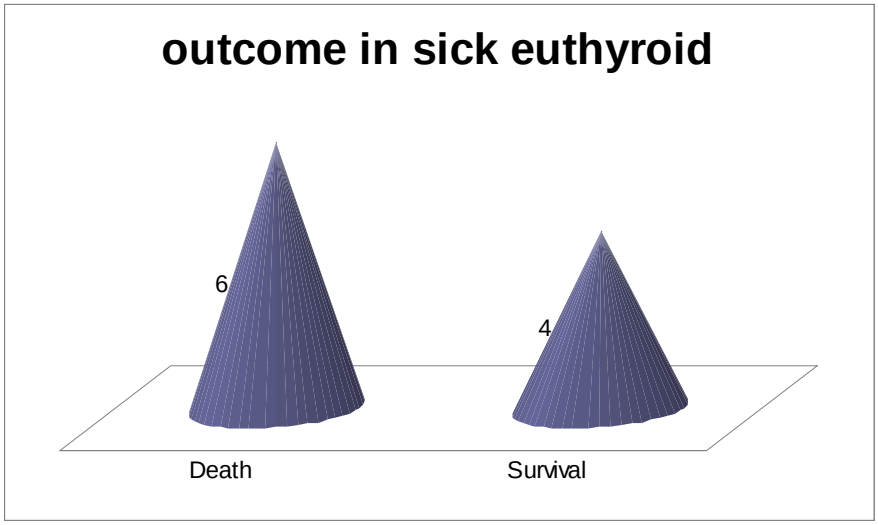
Compound	Nos.	Death
Monocrotophos	16	12
Chlorphyriphos	6	
Phosphamidon	6	1
Prophenophos + Cypermethrin	3	1
Triasophos	3	
Quinalphos	2	1
Chlorphyriphos + cypermethrin	2	
Methylparathion	2	1
Prophenophos	1	
Ethylparathion	1	
Dimethoate	1	
Parathion	1	

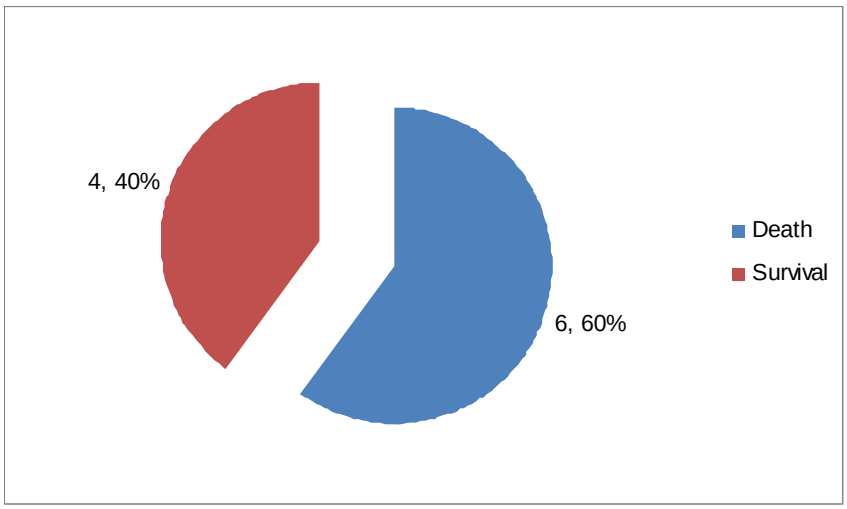


Among the 43 Patients with OPC Poisioning Maximum compound consumed was monochrotophos and death was also maximum in the same.

OUTCOME IN SICK EUTHYROID

	Nos.	Percentage
Death	6	60
Survival	4	40

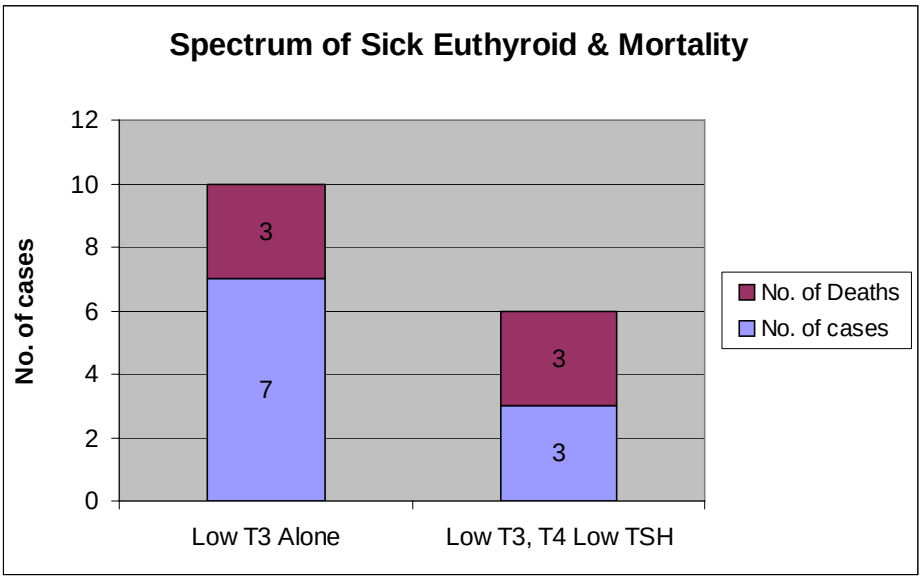


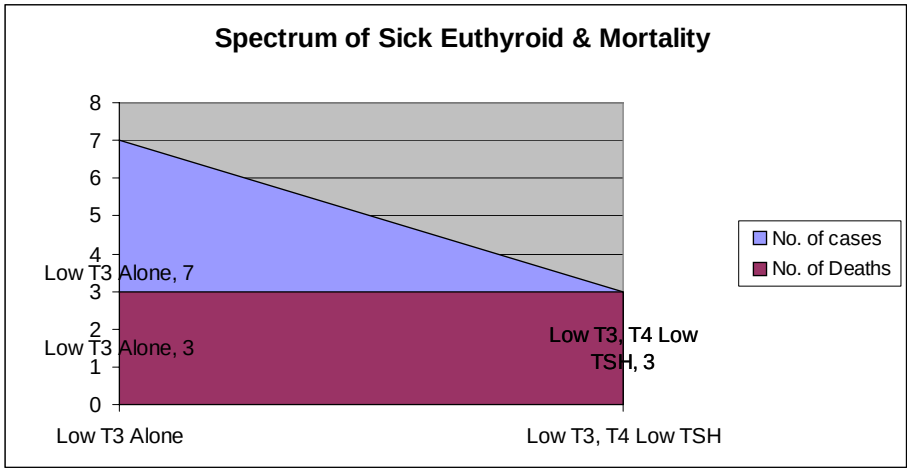


Among the 10 Patients with sick Euthyroid 6 of them expired. The Mortality rate was 60%.

SPECTRUM OF SICK EUTHYROID & MORTALITY

	Nos.	Death
Low T3 Alone	7	3
Low T3, T4 Low TSH	3	3





Among the 10 Patients with sick Euthyroid 6 of them expired. All with changes in T3, T4 & TSH Expired (100%). Those with changes in T3 Alone had a Mortality of 42%

DISCUSSION

Comprehensive analysis of 60 cases of acute organophosphorous poisoning.

EPIDEMIOLOGY OF ORGANPHOSPHOROUS POISONING :

Age Pattern :

In this series of 60 cases, 36 cases were below the age of 30. WHO has reported about 3 million cases of opc exposure and 40,000 detths annually and majority were under the age group of thirty. [30] Murat Sungur and Muhammed Guven et al of turkey observed the mean age group of opc exposure was 30±15 years.[18] Karalliedde L, Senanayake N.et al of SRILANKA documented 91% of their cases were under the age of 30[40]. In Kashmir Valley Malik et al. revealed that 33.5% of the cases of opc were under the age of 25. [41] In Mangalore, Karnataka, India the most common age group to be affected was 20-30 years (36.6%) [30]. The series reported in this thesis had the similar pattern of age group affection. The reason could be that this age group, by all probability, is vulnerable to various emotional conflicts that occur during this phase of life. This young age group affected by exposure form the viable entity of any population both in

terms of procurement and productivity. This case study and the case reports mentioned above throw light on the target age group for educative and preventive programmes to reduce the incidence of opc poisoning.

SEX DISTRIBUTION

In Poison centre GGH Chennai males were exposed more when compared to female population. (58.4% verses 41.6) On the contrary to the series in Murat Sungur Study of 36 cases of opc in Turkey [18] [(female n=25, male =22)] and. Malik et al. Observation of 122 cases in Kashmir valley [(female n=114, male =50)] female intoxication was more [44]. In Srilanka and Mangalore had smilar pattern to the case series of the poison centre. (male 86%-female 14%) S. Shivakumar and K. Raghavan et al of Tamilnadu reported 165 cases of organophosphorous poisoning and sex distribution was similar to the case series (male n=122, female n=45) [38]. This variation was due to handling of poison by the respective sex in their respective locality. In kashmir the female populations are predominantly employed in apple orchards and they are involved in pesticide control. In southern part of India males are actively involved in spraying fertilizers and pesticides.

ROUTE OF EXPOSURE :

Ingestion of the OPC poisoning (n=59) formed the majoriy in this series apart of inhalational (n=1) form of exposure. Arup Kumar Kundu, JD Mukhopadhyay, AK saha, S Das et al [48] studied 108 patients in sub urban West bengal poison, 90 consumed the poison and the death rate was 12% and it had positive correlation with out come. In Kashmir Valley out of 164 cases-ingestional route (n=140), inhalational (n=7) and topical exposure (n=17). In the Turkey study the gastrointestinal route was the main route in 44 (93.6%) Patients.

CLINICAL SEVERITY (MODIFIED DREISHBACH CRITERIA)

In this case series of 60 Cases admitted 49 fell into grade III and II fell into the grade 2 group. The reason could be that this centre being a referral unit, complicated cases, warranting specialist treatment, Intenstive care monitoring, ventilatory support were transfered from primary helath centres, district hospitals and private nursing homes. Arup Kumar Kundu (et.al) reported, mild 15 (14%), moderate 55 (50.9%) and sever 32 (29.6%) in his study based on OPC poisoning in sub-urban West Bengal. In that study, the severe grade of poisoning was associated with increased ventilatory support and poor outcome. Similarly, in this case series, clinical severity association

with need of ventilatory support and mortality was statistically significant. All those with sick Eu Thyroid Syndrome were in grade 3 severity and they were in need of ventilator support.

LAB CONTRIBUTIONS

In this study group, the average total WBC court 8,686 cells cubic mm. (SD.3433). Leukocytosis was also reported in the studies from Turkey and pittsburg. The liver function tests observed in this study had similar pattern of mild elevation when compared to the study from Murat Sungurb et al in TURKEY. Kenneth D. Ketz, et. al who documented metabolic acidosis in his study group.

CHOLINESTERASE LEVELS AND ITS SIGNIFICANCE

In this case study, day 1 ChE correlated very well with clinical criteria of Dreisbach. This finding was also observed by Bobba R, Venkataraman, BV, Pais P, Joseph T. et.al. in Bangalore. In contrary to this observation, S.N. Chugh and Navneeth Agarwal, et.al found no relationship between serum CHE estimation and severity grading. Sequential post exposure estimations of the ChEs up to 3 days revealed significant rise in the values

correlated with substantial clinical improvement. This observation was in par with the study in Bangalore. The Cholinesterase level among those with sick euthyroid was significantly severe than those who were negative.

TREATMENT CONTRIBUTES

In this series, all patients were administrered atropine according to the clinical severity.

In this series, 2PAM was given to all patients, 2PAM was administered at a dose of 500 mg/hr infusion for the first 48 hrs.followed by 1 g IV tds for another 3 days. Arun Kumar kundu, et.al in a study in sub-urban, West Bengal related high dose 2PAM administered in first 24 hours was associated with adverse outcome [48]. In 1991, De Silva studied the treatment of organophosphate poisoning with atropine and 2PAM and, later the same year, with atropine alone. He found that atropine seemed to be as effective as atropine plus 2-PAM in the treatment of acute organophosphate poisoning. The controversy continued when other authors observed more respiratory complications and higher mortality rates with use of high-dose 2-PAM. Studies are underway to assess the role of low-dose 2-PAM [42] S. Shivakumar and K. Raghavan, et. al compated the effectiveness of high dose 2PAM

with low dose by slection of patients in non-random manner. They found out the high dose 2PAM group had better survival, lesser incidence of type 2 paralysis and shortened duration of ventilation.

VENTILATORY SUPPORT

Out of 60 Patients 32 needed ventilatory support. (53%) All patients were initiated on assist contorl mode. 16 out of 32 cases on mechanical ventilation expired. The morality rate among patients on mechanical ventilation was 50%.

Grade 3 clinical severity, proximal muscle affection, low values of day 1 serum ChE were the predictors for the need of mechanical ventilation. Murat Sungur and Muhammed Guven of Turkey in the study of 47 patients of OPC reported mechanical ventilatory support was needed for 10 (21.2%) patients. The duration of mechanical ventilation was 4.1 $\pm$ 3.2 days. The mortality rate for the patients who were mechanically ventilated was 50% (5 patients), although the mortality rate was 27.6% (13 patients) for all patients. The mortality rate for the mechanically ventilated patients was not statistically different compared with those patients not mechanically ventilated. Two patients who are mechanically ventilated died with sudden

cardio respiratory arrest following ventricular tachycardia, and three died from pneumonia and complicating adult respiratory distress syndrome S. Shivakumar and K. Raghavan, et.al. in their case series of 165 patients, 22 patients were mechanically ventilated,out of which 14 died.

INCIDENCE OF SICK EUTHYROID:

Among 60 patients studied,incidence of sick euthyroid was noted in ten patients[17%].Among those with organophosphorous compound poisoning incidence of sick euthyoid was 23%.in study by Guven et al in Turkey out of 22 patients with OPC poisoning sick euthyroid was noted in 7 patients[31.8%]. The Repeat thyroid profile done in 9/10 patients was normal.

COMPOUND AND THYROID STATUS:

Among those with organophosphates the highest incidence was noted among Monocrotophos[50%].the remaining cases were seen among patients with phosphomindon,quinalphos ,methylparathion and parathion.

SPECTRUM OF THYROID STATUS:

In this series of 10 patients of sick euthyoid ,7 had low free T3 alone and 3 had low T3,T4 and TSH.

In the study by Guven et al in Turkey the spectrum of changes observed - 2 had low fT3,2 had fT4 and 3 had low TSH.

OUTCOME ANALYSIS

In this series 16 expired. The mortality rate was 27%. In all cases primary cause of death was respiratory failure with secondary cardiac arrest. It has resulted from central respiratory depression, respiratory muscle weakness, increased bronchial secretions, bronchospasm and acute pulmonary oedema. The prolonged duration of hospital stay, grade 3 clinical serverities, proximal muscle involvement and mechanical ventilation were associated with poor outcome. Karalliedde L, Senanayake N. et.al. reported mortality rate of 18% in their study of 92 cases of OPC in Sri Lanka. Arup Kumar Kundu, JD Mukhopadhyay, AK Saha, S Das Burdwan Medical College and Hospital, Burdwan, West Bengal analyzed that increased time interval before initial atropinisation, higher clinical grading, respiratory paralysis at the time of admission, higher quantity of poison consumed, type of poison (e.g., monocrotophos and dimethoate), poison ingested rather than inhaled, development of encephalopathy and or ECG changes (pulse rate < 45/min, complete heart block QT - Prolongation), and higher

dosage of PAM used in first 24 hours were associated with increased mortaility. In Kahsmire valley a study of 164 patients of OPC Poisoning, the mortality rate was 5.5% In the Mangalore sutdy, the mortality was 26.2 %. Murat Sungur and Muhammed Guven of Turkey reported the mortality rate of 32%.

Among patients with sick euthyoid status [10],6 of them expired and 4 of them survived hence mortality among the patients with sick euthyroid is higher. $p<0.01$. Which is statistically significant.

SUMMARY

Organophosphorous poisoning is a menace to the human race both as a weapon of mass destruction and a misused pesticide of self harm. The case fatality rate exceeds 60% in developing countries where there are many pit falls in treatment protocol and research activities. So a comprehensive analysis of 60 patients of organophosphorous poisoning was done in Poison Centre, Government General Hospital Chennai.

All the cases included in the studied underwent detailed clinical evaluation, extensive laboratory work up and thyroid function status.; Each patient was monitored periodically till the outcome. There were 35 meals and 25 female patients. The predominant age group was 21-30 years.; 59 patients were suicide attempts and one had accidential exposure.; 59 of the patients were poisoned through the gastrointestinal route. One patient had inhalational poisoning. There were 9 different types of OP insecticide agents involved. According to Dreisbach clinical criteria at admission 49 patients belong to the severe grade of poisoning. Serum cholinesterase levels had significant correlation with clinical severity, mechanical ventilation and outcome.

Thyroid Status was assesed for 60 patients. 10 Patients are changes suggestive of sick euthyroid. 6 out of the 10 patients expired. Those who had changes in all three values of thyroid harmone (T3, T4, TSH) had increased mortality

CONCLUSION

1. Pesticide poisoning is more prevalent in the 21 - 30 age group.incidence is more common in males.
2. The most important cause for consumption of organophosphorous poison is self harm.
3. The commonest route of exposure is ingestion of poison and it is associated with increased clinical severity.
4. The duration of stay in the hospital has significant correlation with clinical severity.
5. The higher the clinical grade of poisoning at the inital presentation more the need of ventilatory support and advers outcome.
6. The following parameters predict the need of ventilatory support,grade 3 clinical severity ,proximal mucle weakness,low values of day 1 cholinesterase.
7. The prevalence of sick euthyroid syndrome among individuals with acute pesticide poisoning was 16.5%.
8. Death was high in those with sick euthyroid syndrome.
9. Sick euthyroid syndrome probably reflect the status of toxic effects and /or the susceptible individuals.
10. Probable mechanisms for sick euthyroid syndrome is similar to sick euthyroid syndrome in other critical care illnesses.

RECOMMENDATIONS

To avoid accidental exposure while spraying pesticides,proper precautions should be taken to prevent inhalational and accidental ingestion of the substance.

Insecticedes should be kept out of reach of children,to prevent accidental poisoning.

Improved regulation of the availablity of pesticides,strict regulation of vendors,and modification in packaging of pesticides may all help redcuce the use of organophosphates as poisons.

Adequate provision of information to the public creates awareness about the deleterious effects of OPCs.

Establishment of poison information centres will facilitate in reducing the morbidity and mortality relateed to organophosphorous poisoning.

Many countries like USA, European union ,Thailand banned the production and sales of highly toxic OPCs like Monocrotophos.in Srilanka severe restrictions are enforced over the utilization of Monocrotophos. So the government on India should take necessary steps to restrict the free availablity of highly toxic OPCs like monocrotophos.

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PROFORMA

NAME

AGE

SEX

OCCUPATION

LOCATION

DATE OF ADMISSION

ADMISSION DIAGNOSIS

BRIEF HISTORY

AMOUNT INGESTED

DATE OF INGESTION

TIME OF INGESTION

TIME SINCE CONSUMPTION

SYMPTOMS ON PRESENTATION IN DETAIL:

PRIOR TREATMENT:

PROVIDER:

SUPPORTIVE:

ANTIDOTE:

TIME TAKEN TO REACH FIRST TREATMENT CENTRE:

PERSONAL HISTORY :

PREVIOUS HISTORY OF POISONING [YES / NO] IF YES _DETAILS:
HISTORY OF ALCOHOL AND DRUG ABUSE:IF YES DETAILS:

HIGH RISK BEHAVIOR:

FAMILY HISTORY OF POISONING [YES/NO] IF YES DETAILS:

PHYSICAL EXAMINATION

GENERAL EXAMINATION

VITAL SIGNS

PULSE

RATE

RHYTHM

BP

SYMPTOMATOLOGY

Nausea, Vomiting in case of ingestion

Cough, burning sensation in the chest in case of inhalation

Mild systemic symptoms like headache, dizziness, weakness

Abdominal Pain, diarrhea in case of ingestion

Tightness in chest, difficulty in breathing in case of inhalation

Salivation, Lacrimation, Sweating,

Pupillary Changes

Bradycardia,

Confusion, Tremor, Restlessness.

Respiratory depression, generalized weakness

Cyanosis, peripheral circulatory failure,

Convulsions, Coma.

Intention of the poison :

Suicidal

Accidental

Homicidal

RESPIRATORY RATE

RECTAL TEMPERATURE

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

GASTROINTESTINAL SYSTEM

CENTRAL NERVOUS SYSTEM

GCS

VENTILATORY SUPPORT

INVESTIGATIONS

CBC

- TC
- DC
- PCV
- ESR
- PLATELETS

RFT

- BLOOD SUGAR
- UREA
- SERUM CREATININE
- NA+
- K+

LFT

- TOTAL BILIRUBIN
- AST
- ALT
- SAP
- TOTAL PROTEIN

SERUM CHOLINESTERASE LEVEL

THYROID PROFILE

FREE T3

FREE T4

TOTAL T3

TOTAL T4

TSH

ECG

CHEST X-RAY

TREATMENT

FINAL OUTCOME

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE,CHENNAI-600 003.

Telephone : 25363970

Fax :044 – 253-5115
:044 25363970

I..Dis.No. 14597 /ME5/ thicsDean/MMC/2009 Dated .09.2009

Title of the work : "Sick Euthyroid syndrome in acute pesticide poisoning and prognostic significance"

Principal Investigator : Dr.K. Thirumal valavan, P.G - M.D. Internal medicine

Department : madras medical college, ch - 2

The request for an approval from the Institutional Ethical Committee(IEC) was considered on the IEC meeting held on 23rd September 2009 at 2.00P.M. in Madras Medical College, Deans, Chamber, Chennai-3. / pharmacology Seminar hall, madras medical college ch 2

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The principal investigator and their term are directed to adhere the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of any change of study procedure, site and investigation or guide.
4. You should not deviate form the area of the work for which I applied for ethical clearnance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulations of the institution(s).
7. You should complete the work within the specific period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, MMC,CHENNAI

CHAIRMAN
IEC MMC CHENNAI

21/09/09

DEAN
MADRAS MEDICAL COLLEGE
CHENNAI

S.No.	Age	Sex	Name	Freet3	T4	TSH	Compound	Out Come	Che	Stay	Sug	Urea	Crea	Stay	Sod	Pot	T.B.	Sgot	Sgpt	Severity	Re T3	Re T4	TSH
1	18	f	nirosha	1.08	1.66	0.32	montcro	death	158	3	yes	222	20	0.7	134	2.4	0.7	37	21	3			
2	30	M	manimaran	2	0.97	1.39	phospho	dis	2250	2	no	97	26	0.8	128	3.2	0.9	81	64	3			
3	26	M	satish	1.23	1.28	1.34	qunalphos	dis	318	3	yes	104	34	0.8	126	3.4	0.9	82	21	3	1.92	1.28	1.42
4	22	M	nitharsan	1.24	1.32	1.42	chlorpyrifos	dis	349	1	no	116	28	0.9	124	3.2	0.8	16	26	3			
5	28	M	jegan	2.58	0.98	0.6	chl+cyper	dis	3154	2	no	114	20	0.7	132	4	0.8	21	35	3			
6	13	F	latha	3.4	1.1	2.18	endosul	dis	9856	2	no	72	20	0.7	140	3.9	0.9	26	18	3			
7	41	F	parvathy	1.93	1.11	0.47	montcro	dis	114	3	no	86	16	0.7	143	3	0.8	26	16	3			
8	28	F	lakshmi	1.32	1.14	1.24	prof+cyper	dis	222	7	no	128	17	0.8	130	3.2	0.8	23	20	3			
9	21	M	manikandan	2.8	0.88	1.39	triazpphos	dis	132	13	no	104	26	0.9	131	3.2	0.7	24	28	3			
10	34	M	dharman	2.22	1.17	7.33	cypermethrin	dis	7600	3	no	84	18	0.6	124	2.6	0.9	22	19	3			
11	28	M	gopal	0.92	1.56	0.5	methylparathion	dis	270	24	vent	101	36	0.9	137	3.4	1	60	49	3	2.14	1.58	1.12

S.No.	Age	Sex	Name	Freet3	T4	TSH	Compound	Out Come	Che	Stay	Sug	Urea	Crea	Stay	Sod	Pot	T.B.	Sgot	Sgpt	Severity	Re T3	Re T4	TSH
12	28	M	kumar	0.88	0.76	1.5	monocro	dis	218	18	vent	101	34	1.01	130	3.2	0.9	34	32	3	1.88	1.04	1.52
13	35	M	murugavel	1.98	1.01	0.33	furadion	dis	2839	3	no	94	62	1.2	128	3.2	1	67	38	2			
14	20	M	ravindran	2.87	1.67	1.65	furadion	dis	436	1	no	112	35	0.9	130	3.4	0.8	29	23	3			
15	40	M	ravindran	3.24	1.87	1.1	chlorpyrifos	dis	398	8	no	83	30	0.8	124	3.5	0.8	26	32	3			
16	50	F	chandra	2.04	1.47	0.18	triazpphos	dis	295	3	no	84	20	0.7	130	3	1	24	27	3			
17	14	M	vinothkumar	1.04	1.5	0.34	monocro	death	234	16	vent	150	16	0.7	125	2.8	0.9	106	68	3	1.83	1.52	1.34
18	18	M	deenadayalan	1.12	1.32	0.72	phospho	dis	320	20	vent	211	28	0.8	139	2.9	0.7	48	19	3	1.88	1.34	0.94
19	28	M	jothimurugan	0.18	1.24	0.51	chlorpyrifos	dis	400	13	no	118	18	0.9	127	3.2	0.9	30	28	3			
20	22	F	vijaylakshmi	2.17	1.18	1.2	monocro	death	256	9	no	85	26	0.9	133	4.1	0.9	30	17	3			
21	18	F	megala	0.99	1.2	1.4	monocro	dis	234	23	vent	90	24	0.8	134	4.1	0.8	24	24	3	2.08	1.24	1.48
22	24	m	kumar	2.27	0.83	0.16	furadion	dis	4600	5	no	100	24	0.9	132	3.1	0.9	32	28	2			

S.No.	Age	Sex	Name	Freet3	T4	TSH	Compound	Out Come	Che	Stay	Sug	Urea	Crea	Stay	Sod	Pot	T.B.	Sgot	Sgpt	Severity	Re T3	Re T4	TSH
23	18	F	malathi	0.8	1.29	0.34	methylparathion	death	158	8	vent	98	26	0.8	134	3	0.8	32	30	3	1.14	1.28	1.42
24	28	M	thirupal	4.86	1.57	0.33	furadion	dis	2400	1	no	100	26	1	132	3.4	0.9	30	28	3			
25	25	M	manikandan	0.09	0.92	2.23	prof+cyper	dis	157	5	no	96	24	0.9	132	3.1	1	28	26	3			
26	45	M	vijayan	1.7	0.99	0.19	furadion	dis	876	1	no	100	26	0.8	134	3.2	0.8	32	32	2			
27	20	M	deva	2.86	1.79	0.68	methylparathion	dis	188	4	no	98	24	0.9	132	3.1	0.9	30	28	3			
28	28	M	babu	1.63	1.29	0.55	furadion	dis	1400	3	no	104	26	0.8	134	3.2	0.8	26	24	3			
29	28	M	thangaraj	1.02	1.84	0.42	monocro	death	124	4	vent	98	28	0.9	128	3.4	0.8	28	28	3	1.92	1.8	94
30	38	M	moorthy	0.9	1.64	0.31	profenophos	dis	164	2	no	136	28	0.9	129	2.9	0.9	26	18	3			
31	32	F	maheswari	2.32	1.1	2.43	furadion	dis	390	2	no	112	32	1	132	3.2	0.8	24	24	2			
32	16	F	durgadevi	2.51	1.2	1.94	furadion	dis	384	3	no	114	32	0.8	134	3.8	1	26	28	3			
33	15	F	suganya	2.82	1.87	0.29	triazpphos	dis	3800	2	no	110	34	0.9	136	3.4	0.9	34	40	2			

S.No.	Age	Sex	Name	Freet3	T4	TSH	Compound	Out Come	Che	Stay	Sug	Urea	Crea	Stay	Sod	Pot	T.B.	Sgot	Sgpt	Severity	Re T3	Re T4	TSH
34	15	F	kanagavali	1.95	1.58	0.54	chlorpyrifos	dis	143	5	no	104	32	0.8	134	3.2	0.8	32	32	2			
35	25	m	pushparaj	1.08	1.32	0.62	cypermethrin	dis	132	13	no	110	34	0.8	132	3.2	0.9	32	30	2			
36	32	M	jaiganesh	1.9	2.1	0.8	monocroto	dis	308	8	no	108	32	0.9	131	3.2	0.8	3	3	3			
37	40	M	palanivel	0.8	0.9	0.6	monocro	death	118	3	no	110	28	0.8	132	3.3	1.1	34	36	3			
38	28	M	kALIDAS	1.4	1.8	0.8	chlorpyrifos	dis	408	2	no	104	26	0.9	131	3.2	0.8	34	36	3			
39	16	F	iswarya	0.9	1.9	1.14	monocro	death	150	3	no	100	24	0.8	132	3.4	0.8	32	30	3			
40	25	M	karthik	1.8	2.24	2.3	chlorpyrifos	dis	600	14	no	104	26	0.8	132	3.2	0.9	34	40	2			
41	55	M	lakshmanan	1.1	2.23	2.34	monocro	death	112	18	no	104	32	1.2	134	3.3	1	32	34	3			
42	30	F	sivagami	1.9	2.23	2.23	monocro	death	116	2	no	106	34	1.8	137	3.4	0.8	28	30	3			
43	35	M	gopi	1.8	2.42	2.08	monocro	death	132	4	no	104	38	0.4	136	3.4	0.9	26	30	3			
44	26	M	satish	1.8	2.3	2.4	chlorpyrifos	dis	1400	2	no	100	32	1.2	138	3.2	0.8	26	28	3			

S.No.	Age	Sex	Name	Freet3	T4	TSH	Compound	Out Come	Che	Stay	Sug	Urea	Crea	Stay	Sod	Pot	T.B.	Sgot	Sgpt	Severity	Re T3	Re T4	TSH
45	50	M	palani	1.08	1.9	2.3	phosphomindon	death	132	19	no	88	30	1.2	136	3.1	0.8	30	32	3			
46	18	F	nirosha	0.8	1.9	2.23	monocro	death	112	20	no	90	40	0.9	132	3.4	0.9	28	32	3			
47	27	F	usha	1.9	2.2	2.34	ethylparathiion	dis	346	3	no	98	24	0.8	133	3.3	1.1	44	42	3			
48	34	M	sampath	1.8	2.3	2.24	dimethoate	dis	6000	2	no	100	28	0.9	132	3.2	1.2	48	42	3			
49	47	M	vengatesan	1.78	2.3	2.1	quinalphos	death	208	11	no	106	29	0.8	134	3.3	0.9	38	42	3			
50	18	M	nithiyanadan	1.09	2.23	2.8	phosphomindon	death	112	10	no	100	28	0.8	135	3.4	0.8	36	36	3			
51	28	F	lakshmi	0.1	2.2	1.98	prof+cyper	dis	234	3	no	102	26	0.9	132	3.2	0.9	32	33	3			
52	37	F	manjula	1.08	1.23	0.24	furadian	dis	3200	1	no	86	28	0.9	134	3.3	0.8	32	34	3			
53	18	F	bala	0.7	1.32	1.24	demecran	dis	142	25	vent	100	28	0.8	135	3.4	1.1	44	42	3	1.84	1.32	1.24
54	50	M	allimuthu	1.09	2.24	2.3	monocroto	death	116	9	no	86	28	0.9	134	3.2	0.9	42	40	3			
55	17	F	durgalakshmi	1.08	2.03	2.24	furadion	dis	3200	2	no	88	24	0.9	135	3.3	0.9	42	40	2			

S.No.	Age	Sex	Name	Freet3	T4	TSH	Compound	Out Come	Che	Stay	Sug	Urea	Crea	Stay	Sod	Pot	T.B.	Sgot	Sgpt	Severity	Re T3	Re T4	TSH
56	31	M	elumalai	1.12	2.12	2.24	monocro	death	124	5	no	104	32	0.9	136	3.4	1.1	32	34	3			
57	15	F	priya	1.08	2.21	2.08	furadion	dis	1800	3	no	126	34	0.8	134	3.2	0.9	34	36	2			
58	20	F	chitra	1.12	2.08	2.21	pyrethroid	dis	3400	1	no	114	32	0.9	131	3.3	1.1	32	30	2			
59	24	M	ramesh	1.08	2.12	2.14	cypermethrin	dis	212	8	no	118	34	0.8	131	3.2	0.9	34	34	3			
60	19	F	sathya	1.09	2.14	2.22	phosphomindon	dis	312	7	no	104	32	0.9	132	3.3	0.8	36	34	3			